REMARKS

Claims 5-16 remain in the application. Claims 15 and 16 are currently withdrawn from consideration due to the earlier restriction requirement (which is addressed herein). Claims 15 and 16 have been amended herein to include a Roman number designation for the chemical structure. Claim 16 has been amended to address the claim numbering discrepancy noted by Examiner Kumar.

Claims 7, 8, and 9 have been amended herein to be independent claims. Several additional trifluoro-substituted compounds have been added to Claim 7. These claims are supported by Claim 5 has originally filed.

Restriction Requirement:

Applicants confirm their prior election, **with traverse**, to prosecute Claims 5-14.

Restriction is proper only if the restricted claims are independent or patentably distinct and there is no serious burden placed on the Examiner if restriction is not required (MPEP §803). The burden is on the Examiner to provide reasons and/or examples to support any conclusion of patentable distinctness between the restricted claims (MPEP §803). Applicant respectfully traverses the restriction requirement on the grounds that the Office has not carried the burden of providing any reasons and/or examples to support the conclusion that the claims of the restricted groups are, in fact, distinct.

The Office has characterized the claims as not relating to a single general inventive concept under PCT Rule 13.1. However, in the corresponding PCT application, there was no finding of lack of unity of invention. Thus, there should not be a restriction requirement in the present claims. For claims to be found unrelated for purposes of restriction under US law (which appears to be the Office's position in this instance), the Office must show **both** that the claims are not disclosed as capable of use together **and** they have different modes of operation, different functions, or different effects. Applicants traverse the restriction requirement because the Office has not shown how its stated examples amount to different modes of operation, different functions, or different effects; nor has the Office articulated how the claims are incapable of use

together. Consequently, because the Office has not carried its burden to establish that the groups of claims as identified by the Examiner are unrelated, Applicants submit that the restriction requirement is improper. Applicants therefore traverse the restriction requirement and request that it be withdrawn.

Rejection of Claims 11-13 Under 35 USC §112, First Paragraph (Enablement):

This rejection is respectfully traversed because one of ordinary skill in the art can practice the invention as broadly as it is claimed without resorting to any undue experimentation or testing.

For example, Claim 13 is directed to a method of activating histone acyletransferases in a patient. This is done simply by administering the recited compounds to the patient, by any suitable route well known in the art of pharmacy. Regarding suitable routes for administering a pharmaceutical agent to a patient, a host of such routes are conventional and exceedingly well-known to those of ordinary skill in the art (*e.g.*, oral, intravenous, intramuscular, etc.). What is well-known in the art is best omitted from the specification. See MPEP §2164.08 and *In re Buchner*, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991). Regarding the amount to be delivered that is effective to activate histone acetyltransferases (HATs), the specification includes a description of an assay to measure HAT activity. See the discussion starting at page 14, line 13. (Note also that there are a number of other HAT assays known in the literature; see reference 13 in the application as filed.) Therefore, to optimize a specific dosage of a claimed compound for a specific patient, one simply establishes a baseline HAT activity in the patient (using the assay described in the specification) and then administers increasing large dosages of the compound to the patient until HAT activity is increased. Such an approach is standard practice in the field of pharmacy. For example, coumadin, a widely prescribed blood thinner, is prescribed in the same fashion. The patient is treated with an initially low dose and the dose is then monitored for its blood-thinning results. The dose is then increased or decreased accordingly. This type of dose adjustment, however, is totally routine. It does not constitute **undue** experimentation.

Regarding claims 11 and 12, Applicants explicitly traverse the Office's citation to *In Re*

Fisher, 166 USPQ 18 (CCPA 1970) as standing for the proposition that each embodiment within a Markush group must be "individually tested" for physiologic activity (see middle of page 5 of the Office Action). That's simply not the holding of the *Fisher* case; nor does the *Fisher* case stand for such an exacting level of enablement. Quite to the contrary, the Fisher case clearly articulates that §112, first paragraph requires only that the scope of the claims "bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art." See 166 USPQ at page 24. Moreover, the position advanced by the Office with respect to enablement is flatly contradicted by later, controlling cases from the Court of Customs & Patent Appeals and its successor court, the Court of Appeals for the Federal Circuit. Specifically, there's no requirement that Applicants even make the claimed compounds or provide a working example (much less test all of them) in order to enable the claims. See *In re Robins*, 166 USPQ 552 (CCPA 1970). Further, *In re Angstadt*, 190 USPQ 214 (CCPA 1976) explicitly held that Applicants **do not** have to make and test all of the species within a generic claim in order to enable the generic claim. Both the *Robins* case and the *Angstadt* case were cited **with approval** by the Court of Appeals for the Federal Circuit in *Amgen v. Chugai*, 18 USPQ2d 1016 at page 1027 (CAFC 1991). Citing to the *Angstadt* case, the *Amgen* court explicitly stated that "It is **not** necessary that a patent applicant test all the embodiments of his invention." (Emphasis added.) At the same page, and citing to the *Robins* case, the *Amgen* court further stated "A specification may, within the meaning of §112, first paragraph, contain a written description of a broadly claimed invention **without** describing all species that claim encompasses.... [R]epresentative samples **are not** required by the statute and are not an end in themselves." (Emphasis added.) See also §2164.03: "The scope of the required enablement varies inversely with the degree of predictability involved, but even in unpredictable arts, a disclosure of every operable species **is not** required." Emphasis added. In short, Applicants submit that this rejection is improper because the Office is holding Applicants to an improperly high standard for purposes of satisfying the enablement requirement of §112, first paragraph.

Applicants also explicitly traverse the statement at the bottom of page 5 of the Office Action that states "There is no proof that the claimed compounds have ever been administered to

a human." On whom would the Office have Applicants run the initial human testing? Prisoners? The compounds have not yet even been submitted to the FDA for approval for human testing. Again, Applicants submit that this rejection is clearly improper because the Office is advancing a standard for §112 enablement that has no basis in the statutes, regulations, MPEP, or case law. There is no requirement that Applicants test a pharmaceutically active agent on either human subjects or animal subjects to satisfy the enablement requirement. On this point, please see MPEP §2164.02 and the cases cited therein. Most notably, the following passage addresses the present issue:

> "Correlation' as used herein refers to the relationship between *in vitro* or *in vivo* animal model assays and a disclosed or a claimed method of use. An *in vitro* or *in vivo* animal model example in the specification, in effect, constitutes a "working example" if that example "correlates" with a disclosed or claimed method invention. If there is no correlation, then the examples do not constitute "working examples." In this regard, the issue of "correlation" is also dependent on the state of the prior art. In other words, if the art is such that a particular model is recognized as correlating to a specific condition, then it should be accepted as correlating unless the examiner has evidence that the model does not correlate. See *In re Brana*, 51 F.3d 1560, 1566, 34 USPQ2d 1436, 1441 (Fed. Cir. 1995) (**reversing** the PTO decision based on finding that *in vitro* data did not support *in vivo* applications).

Applicants have included with their application a number of assays that show that the claimed compounds are HAT activators. See Fig. 4 and the paragraph at page 27, lines 22-25 of the application as filed. These *in vitro* data clearly correlate administering the claimed compound to an increase in HAT activity. As noted at pages 1 and 2 of the application, HAT enzymes are known to play a key role in a host of disease states, notably cancer and HIV infection. Thus, having shown a clear correlation between the claimed compounds and their HAT-activating pharmacological activity, Applicants submit that they have satisfied the enablement requirement of §112, first paragraph.

Lastly, Applicants note that they **are not** claiming a cure for cancer or for AIDS, but simply a treatment for these diseases.

In light of the above remarks, Applicants submit that the rejection of Claims 11-13 under 35 USC §112, first paragraph (enablement) is untenable. Withdrawal of the rejection is

respectfully requested.

Rejection of Claims 5-6, 10, and 14 Under 35 USC §102(b) Over U.S. Patent No. 3,113,067 ("the '067 Patent"):

This rejection has been overcome by appropriate amendment to Claims 5 and 6. Specifically, the nitro substituent (NO_2) as a possibility for any of R^3-R^7 has been deleted from Claims 5 and 6. Applicants note that this draws a very clear distinction between the claimed compounds and those described in the '067 Patent because column 1, lines 24-27 of the '067 Patent explicitly states, without reservation, that "at least one of R_4 denotes a nitro group." The presently amended claims do not read on these compounds because a nitro group is not contained in any of the Markush groups recited in Claims 5 and 6.

With respect to Claim 10, because this claim recites a method of making the compounds recited in Claim 5, Applicants submit that the amendment to Claim 5 renders Claim 10 free of this rejection. Claim 5 does not recite any compounds described in the '067 Patent.

As applied to Claim 14, Applicants submit that the rejection has been overcome, in major part, by the above amendment, and is, in minor part, respectfully traversed. As noted earlier, Claims 5 and 6 have been amended to recite a set of compounds that are not disclosed by the '067 Patent. Thus, this rejection has been overcome in major part. Applicants traverse the rejection, in part, because Claim 14 is drawn to a pharmaceutical composition for treating various disease states. In contrast, the '067 Patent is directed to a pesticide for killing snails and slugs. Applicants submit therefore that the composition recited in Claim 14 (a composition for treating various diseases) is distinctly different from the pesticide described in the '067 Patent.

In light of the amendment to Claims 5 and 6 and the above comments, Applicants submit that the rejection of Claims 5-6, 10, and 14 under §102(b) in view of U.S. Patent No. 3,113,067 has been overcome. Withdrawal of the rejection is respectfully requested.

Rejection of Claims 5-10 and 14 Under 35 USC §103(a) Over U.S. Patent No. 3,113,067 ("the '067 Patent"):

As applied to Claims 5, 6, 8-10, and 14, this rejection is believed to have been overcome by appropriate amendment to the claims. Specifically, Claims 5, 6, 8 and 9 have been amended to omit from their scope compounds substituted with a nitro group. Claims 10 and 14 depend from Claim 5. There is no motivation to alter the compounds described in the '067 Patent to arrive at the compounds recited in Claims 5 and 6 because the '067 Patent explicitly states that one of the R^4 groups described therein **must** be a nitro group. See the '067 Patent col. 1, lines 24-27. Because the '067 Patent requires a nitro group for the compounds described therein to have their stated utility (a pesticide to kill snails and slugs), there is no technological motivation to alter the compounds because to do so would destroy the anti-gastropod utility cited within the '067 Patent (see col. 1, lines 20-30). It is well-settled law that a *prima facie* case of obviousness is not present when the modification proposed by the Office destroys the utility of the invention described in the applied prior art reference. See *In re Gordon*, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984) and MPEP §2143.01. Thus, as applied to Claims 5, 6, 8, and 9, Applicants submit that this rejection has been overcome.

As applied to Claim 7, this rejection is respectfully traversed. Applicants note that there are two fundamental differences between **all** of the compounds recited in Claim 7 and the compounds described in the '067 Patent. First, all compounds recited in Claim 7 require that the R^2 substituent be an alkyl group. That is, all of the compounds recited in Claim 7 are 2-alkoxy-substituted benzamides. This type of compound is neither taught, nor suggested by the '067 Patent because the '067 Patent requires either a hydrogen or an aliphatic acyl group at this same position (*i.e.*, R^1 of the '067 Patent). The '067 Patent neither describes nor suggests using an 2-alkoxy-substituted benzamide. Second, **all** of the compounds recited in Claim 7 require a 3-position trifluoromethyl group on the phenyl ring. The '067 Patent is totally silent with respect to substituting the phenyl ring with a perfluoro substituent.

As noted earlier, there is no motivation to alter the compounds described in the '067 to arrive at the compounds recited in Claim 7 because to do so would destroy the anti-gastropod utility articulated by the '067 Patent. Applicants therefore respectfully submit that the rejection of Claim 7 under §103(a) in view of the '067 Patent is improper.

As applied to Claim 14, which is drawn to a pharmaceutical composition to treat various disease states, Applicants note that the '067 Patent is directed to a pesticide to kill snails and slugs. Thus, the '067 Patent is clearly non-analogous prior art to a pharmaceutical composition to treat, for example, cancer or HIV infection. One skilled in the art of pharmaceuticals simply would not look to the field of anti-gastropod pesticides in search of promising compounds to treat cancer in mammals, including humans. Applicants respectfully submit that the Office is engaging in 20/20 hindsight – using Applicants' own specification to guide it through the prior art. But it is the prior art itself that must suggest the modification required to arrive at the claimed invention. The Office is not allowed to use Applicants' own specification to provide the motivation that is lacking in the applied prior art. The '067 Patent is directed solely to a pesticide, not a pharmaceutical composition. The '067 Patent is totally silent with respect to treating any disease state in any animal. Thus, as applied to Claim 14, this rejection is improper because there is no teaching or suggestion of a pharmaceutical composition within the '067 Patent.

In light of the amendment to the claims and the above remarks, Applicants submit that the rejection of Claims 5-10 and 14 under §103(a) over U.S. Patent No. 3,113,067 has been overcome. Withdrawal of the rejection is respectfully requested.

CONCLUSION

Applicants submit that the application is now in condition for allowance. Early notification of such action is earnestly solicited. The Commissioner is authorized to charge any fees or credit any overpayments relating to this application to deposit account number 18-2055.

Submitted for the Applicant,

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